

REMARKS

Reconsideration and allowance of all pending claims is respectfully requested.

Status of Claims

Claims 1-4, 6-8, 10-12, 14-16, 18-20, 22-24, 26-28, 30-32, 34-36, 38-40, 42-44, 46-48, 50-52, 54-56, 58-60, 62-64, 66-68, 70-72, 74-76, 78-80, 82-84, 86-89, 91-93, 95, 96, 98-111, 113-115, 117-119, 122-124, 127-131, 133, 137-141, 144, and 146-205 are pending. No claim is amended or cancelled herein.

35 U.S.C. § 103(a)

Reconsideration is requested of the rejection of claims 1-4, 6-8, 10-12, 14-16, 18-20, 22-24, 26-28, 30-32, 34-36, 38-40, 42-44, 46-48, 50-52, 54-56, 58-60, 62-64, 66-68, 70-72, 74-76, 78-80, 82-84, 86-89, 91-93, 95, 96, 98-111, 113-115, 117-119, 122-124, 127-131, 133, 137-141, 144, and 146-205 under 35 U.S.C. § 103(a) as being unpatentable over Menichincheri et al. (WO 96/14308).

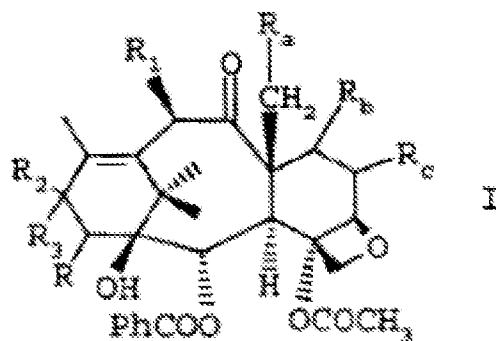
For claimed subject matter to be *prima facie* obvious under 35 U.S.C. § 103(a) in view of prior art, the prior art references must individually or in combination disclose or suggest all of the elements of the claim. Furthermore, there must be a reason for combining the elements in the manner claimed.¹

Claim 1 is directed to taxanes having a C(10) ester substituent, R_{10a}COO-, wherein R_{10a} is hydrocarbyl, substituted hydrocarbyl, or heterocyclo, wherein said hydrocarbyl or substituted hydrocarbyl contains carbon atoms in the alpha and beta positions relative to the carbon atom of which R_{10a} is a substituent, and said heterocyclo is bonded to the carbonyl carbon of R_{10a}COO- through a ring carbon atom. The taxanes of claim 1 also possess a C(13) ester side chain.

Menichincheri et al. generically disclose taxanes having a wide variety of C(6), C(7), C(8), C(10), and C(14) substituents. Importantly, however, the compounds of Menichincheri et al. have **an aza or imine substituent at C(13)**.²

¹ M.P.E.P. §§ 2143-2143.03 and KSR International Co. v. Teleflex Inc., 127 S.Ct. 1727, 1742 (2007).

² Menichincheri et al., pages 2-5.



[wherein] [...]

(i) R₂ and R₃ together represent a group of the formula A-N=, as pure E or pure Z isomers or as a mixture of both E and Z isomers, wherein A represents:

$$[\dots]$$

or

(ii) R_2 represents a group of the formula $B-NH-$ wherein B represents

[...].

The C(13) aza or imine element was at the center of Menichincheri et al.'s invention; they were substituting an aza or imine substituent at C(13) for the conventional C(13) ester in an effort to produce "more potent compounds having the broadest possible spectrum of activity on different cancer types."³

As recently held by the Supreme Court, the Office must articulate a sufficient rational underpinning to (i.e., express reasons supporting) the legal conclusion of obviousness. This requirement was expressed by the Supreme Court in *KSR International Co. v. Teleflex Inc.*, in which the court approved the holding of *In re Kahn*: To facilitate with review, this analysis should be made explicit.⁴ In this case, the Office

³ Menichincheri et al., pages 1-2.

⁴ *KSR International Co. v. Teleflex Inc.*, 127 S.Ct. 1727, 1740-1741 (2007); *In re Kahn*, 441 F.3d 977, 988 (Fed. Cir. 2006) (“[R]ejections on obviousness grounds cannot be sustained by mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness.”).

must expressly state a reason why the ordinarily skilled person would have modified Menichincheri et al.'s C(13) aza or imine compounds to arrive at applicants' claimed C(10), C(13) esters.

In addition, the Supreme Court in *KSR* approved the holding of *United States v. Adams*:

As is clear from cases such as *Adams*, a patent composed of several elements is not proved obvious merely by demonstrating that each of its elements was, independently, known in the prior art. Although common sense directs one to look with care at a patent application that claims as innovation the combination of two known devices according to their established functions, ***it can be important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed invention does.***⁵

The Office's obviousness rejection rests *solely* on the assertion that:

Menichincheri et al. ... teach taxane compounds corresponding to formula (I) where, for example, R₁ [i.e., C(10)] is OCOR', wherein R' is C₃-C₆ cycloalkyl, and R₂ [i.e., C(13)] is B-NH- where B is Y and Y is a carbamate. [...] Other closely structurally relating (sic) compounds would have likewise been obvious to one of skill in the art as the results would not have been unexpected.⁶

It is submitted that this assertion is a mere conclusory statement and does not provide a sufficient rational underpinning showing why the ordinarily skilled person would have modified Menichincheri et al. to arrive at the applicants' claimed compounds. Rather, the reference discloses such widely different compounds that the ordinarily skilled person would not have found any reason to modify the cited reference to arrive at the compounds defined by the instant claims.

Furthermore, it is well established that a prior art reference must be considered in its entirety, i.e., as a **whole**, including portions that would lead away from the claimed

⁵ *KSR International Co. v. Teleflex Inc.*, 127 S.Ct. 1727, 1741 (2007) .

⁶ Office action dated May 9, 2008, page 4.

invention.⁷ The different goals of the cited reference (i.e., C(13) azas and imines) result in sharp differences between the reference and the claimed compounds that cannot be ignored when assessing the purported obviousness of the claims.

According to Menichincheri et al., their C(13) aza or imine taxanes could also possess a wide range of alternative substituents at other positions of the taxane. For example, they suggest a wide range of possible alternative substituents at each of C(6), C(7), C(8), C(10), and C(14). Importantly, however, they attach ***no particular significance*** to any of these alternative substituents; notably, none of the compounds prepared by Menichincheri et al., as detailed in the working examples, have anything other than a hydroxy or acetoxy (i.e., -OC(=O)-CH₃) substituent at C(10), the conventional C(10) substituents on the 10-deacetyl baccatin III and baccatin III starting materials. In contrast, where a hydrocarbyl or substituted hydrocarbyl substituent is selected for R_{10a} in claim 1, (i.e., where R₁₀ is R_{10a}COO- and R_{10a} is hydrocarbyl or substituted hydrocarbyl), the claim requires carbon atoms in the alpha ***and beta*** positions relative to the carbon atom of which R_{10a} is a substituent. Moreover, the claims require a C(13) ester side chain, whereas Menichincheri et al. lead in a new direction: C(13) aza and imines.

Furthermore, Menichincheri et al. fail to provide *in vivo* or *in vitro* data for any of their C(13)-aza or -imine compounds, regardless of the substitution pattern elsewhere on the compound, nor do they compare any of their compounds with other conventional taxanes such as paclitaxel or docetaxel.

According to the rationale proffered by the Office in support of its obviousness rejection, one of skill must pay **strict attention** to the C(10) position and the laundry list of possible alternative substituents at that position, even though Menichincheri et al. provide *no guidance* which would lead one of skill to anything other than the conventional C(10) substituents (i.e., hydroxy and acetoxy) present on the precursor compounds. And yet, one of skill must **ignore** the one element that Menichincheri et al.

⁷ M.P.E.P. § 2141.02(VI) (citing *W.L. Gore and Associates, Inc. v. Garlock, Inc.*, 721 F.2d 1540, 220 USPQ 303 (Fed. Cir. 1983), *cert. denied*, 469 U.S. 851 (1984)).

believe is critical - - the C(13) aza or imine side chain - - in order to select a C(13) ester side chain. The Office does not, and indeed cannot, reconcile this divergent path.

Simply put, the line of reasoning asserted by the Office does not support a finding of *prima facie* obviousness. There is no data or even working examples directed to compounds other than C(10) hydroxy or acetoxy, and Menichincheri et al.'s singular focus is on C(13) nitrogen-containing compounds. Stated differently, Menichincheri et al. were going in a direction *away* from C(13) esters. Thus, the facts and underlying evidence would not lead one of skill to the claimed compounds, nor could one of skill have predicted that the resulting taxanes having the C(10) and C(13) ester substituents would have pharmaceutical efficacy. Hence, the Office's findings regarding obviousness fall short.

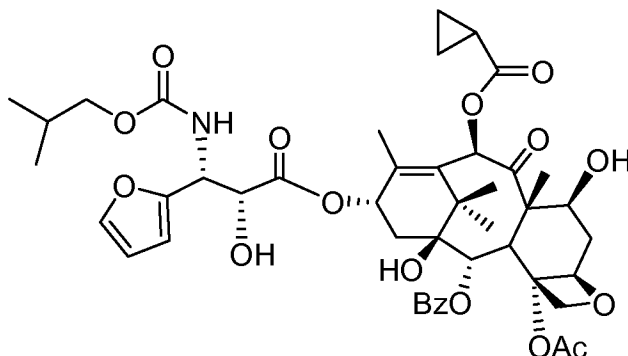
Without more, it is submitted that a person of ordinary skill would not have found the instant claims obvious without use of impermissible hindsight reconstruction using applicants' disclosure as a template.⁸ Thus, without the benefit of hindsight, there is no motivation to select a C(13) ester, in general, regardless of the substitution pattern of the remaining compound, or a C(10) ester having a hydrocarbyl or substituted hydrocarbyl moiety with carbon atoms alpha and beta to the carbonyl carbon, based on the compounds described in the cited references. For these reasons and those set forth in further detail above, it is respectfully submitted that claim 1 is patentable over the cited references, alone or in combination.

Claims 2-4, 6-8, 10-12, 14-16, 18-20, 22-24, 26-28, 30-32, 34-36, 38-40, 42-44, 46-48, 50-52, 54-56, 58-60, 62-64, 66-68, 70-72, 74-76, 78-80, 82-84, 86-89, 91-93, 95, 96, 98-111, 113-115, 117-119, 122-124, 127-131, 133, 137-141, 144, and 146-205 each depend from or are similar to claim 1 and are not obvious in view of Menichincheri et al. for the same reasons as those stated with respect to claim 1. In addition, each of these claims introduce further requirements and the Office has not even attempted to make out a *prima facie* case of obviousness with respect to these claims. For instance, various claims require the C(3') position on the side chain (designated as X₃) to be

⁸ According to M.P.E.P. § 2141(III)(C), the references must be viewed without the benefit of impermissible hindsight vision afforded by the claimed invention (citing *Hodosh v. Block Drug Co., Inc.*, 786 F.2d 1136, 1143 n.5, 229 USPQ 182, 187 n.5 (Fed. Cir. 1986)).

2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, and/or 4-pyridyl. While Menichincheri et al. includes broad disclosure directed to heteroaryl-substituted aza or imine C(13) side chains, the compounds in their working examples are all phenyl-substituted at the relevant position.

By way of another example, claim 175 is directed to a taxane having the formula:



There is no evidence or suggestion in Menichincheri et al. of a taxane having such a configuration. See also, for example, claims 155 and 161-164.

Provisional Double Patenting Rejection

Reconsideration is respectfully requested of the provisional obviousness-type double patenting rejection of claims 1-4, 6-8, 10-12, 14-16, 18-20, 22-24, 26-28, 30-32, 34-36, 38-40, 42-44, 46-48, 50-52, 54-56, 58-60, 62-64, 66-68, 70-72, 74-76, 78-80, 82-84, 86-89, 91-93, 95, 96, 98-111, 113-115, 117-119, 122-124, 127-131, 133, 137-141, 144, and 146-205 over the claims of copending U.S. Patent Application Serial No. 11/057,703.

The analysis employed in an obvious-type double patenting rejection parallels the guidelines of a 35 U.S.C. § 103 obviousness determination.⁹ However, an important distinction exists. A rejection for obviousness must be based on a comparison of the claimed invention to the entirety of the disclosure in the prior art reference, whereas an

⁹ *In re Braat*, 937 F.2d 589 (Fed. Cir. 1991).

obviousness-type double patenting rejection must be grounded on a comparison of the claimed invention to the claims, **and only the claims**, of the reference.¹⁰

It is respectfully submitted that the subject matter of the claims of the present application would not have been obvious in view of the claims of U.S. Patent Application Serial No. 11/057,703. When evaluating the scope of a claim, every element of the claim must be considered.¹¹ To support an obviousness-type double patenting rejection, the claims must have been obvious at the time of filing and not merely obvious upon hindsight reconstruction using applicants' disclosure as a template to arrive at the features of the instantly claimed methods from the claims of U.S. Patent Application Serial No. 11/057,703. It is respectfully submitted that the Office has failed to establish obviousness based on these references, or by evidence of the level of skill in the art or the nature of the problem, that is not based upon impermissible hindsight reconstruction.

In any event, the two applications are pending and, thus, the obviousness-type double patenting rejection is only provisional. Upon a finding of allowable subject matter in this application, the earlier-filed application, the double patenting rejection may properly be withdrawn. See M.P.E.P. 804[I][B].

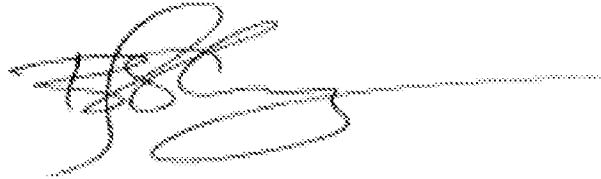
¹⁰ *Purdue Pharma L.P. v. Boehringer Ingelheim GmbH*, 98 F.Supp.2d 362, 392, 55 USPQ2d 1168, 1190 (S.D.N.Y. 2000), *aff'd*, 237 F.3d 1359, 57 USPQ2d 1647 (Fed. Cir. 2001).

¹¹ See, e.g., *In re Ochiai*, 71 F.3d 1565, 1572, 37 USPQ2d 1127, 1133 (Fed. Cir. 1995).

CONCLUSION

In view of the foregoing, favorable consideration and allowance of claims 1-4, 6-8, 10-12, 14-16, 18-20, 22-24, 26-28, 30-32, 34-36, 38-40, 42-44, 46-48, 50-52, 54-56, 58-60, 62-64, 66-68, 70-72, 74-76, 78-80, 82-84, 86-89, 91-93, 95, 96, 98-111, 113-115, 117-119, 122-124, 127-131, 133, 137-141, 144, and 146-205 is requested. The Examiner is invited to contact the undersigned should any issue remain unresolved. The Commissioner is hereby authorized to charge to Deposit Account No. 02-4467 any fees under C.F.R. §§ 1.16 and 1.17 which may be required during the pendency of this application.

Respectfully submitted,

A handwritten signature in black ink, appearing to read 'B. Sodey', with a long horizontal line extending to the right.

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